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Patent Application

**LITERAL ENGLISH TRANSLATION OF
INTERNATIONAL APPLICATION
PCT/EP2005/001460**

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Anti-wrinkle cosmetic

10 The invention relates to a novel anti-wrinkle cosmetic based on natural plant extracts.

It is known to use plant extracts in cosmetic products. Surprisingly, the overall effect resulting from combinations of
 15 several plant extracts is often different from the individual effects and also depends on the parts of the plants selected and the extractants used. Poppy (*Papaver*) is in most cases known for its internal effects only, due to its alkaloid content. *Passiflora* extracts have, in general, also been used internally
 20 as an anti-spasm or anti-inflammatory agent. EP 1002524 B1 describes a mixture of musk rose oil, camellia oil and sunflower oil, which can also contain passion flower oil, as an anti-ageing agent. Mint (*Mentha*) has in particular been used externally so far, for treating irritations of the skin or, combined
 25 with other plants, for skin-whitening (WO 02/065999). WO 03/083028 describes a body cleanser containing *Mentha spicata* var. *viridis* as active agent.

The object of the invention is to provide a cosmetic for reducing wrinkles which at the same time has a silky texture when
 30 being applied, without the additives normally used for this purpose, improves the skin's elasticity and has a long-lasting moisturizing effect.

35 According to the invention, the anti-wrinkle cosmetic consists of a W/O silicone oil system and comprises the following active ingredients (in % by weight and relative to the cosmetic's total weight)

0.05 to 3 % of an extract from *Papaver*,
 40 0.05 to 2 % of an extract from *Passiflora*,

0.05 to 3 % of an extract from *Mentha*,
0.05 to 3 % of an extract from *Myrtus*,
in addition to usual cosmetic auxiliaries, carriers, active
agents or mixtures thereof, which make up the remainder up to
5 100 %.

It has been found that a combination of the four aforesaid
specific plant extracts has an anti-wrinkle effect on human skin
and also enables significant improvements as regards fine lines
10 in elderly skin.

In addition to the active ingredients mentioned above, the
cosmetic can preferably contain 0.5 to 15 % by weight of a solu-
tion of the hexapeptide acetyl-Glu-Glu-Met-Gln-Arg-Arg-NH₂, the
15 concentration of the pure peptide in said solution being
0.5 g/l. Contents of 0.5-2.0 % by weight are particularly pre-
ferred. Surprisingly, the anti-wrinkle effect of the inventive
combination of plant extracts is enhanced by the addition of the
aforesaid hexapeptide, which probably inhibits the excessive
20 production of catecholamines to which the formation of wrinkles
can be put down.

It is preferred that the conditioned extract from *Papaver* be an
extract from *P. rhoeas*, *P. adulis*, *P. incarnata*, *P. laurifolia*,
25 *P. quadrangularis*, *P. somniferum* or mixtures thereof. Said
Papaver extract is an extract obtained from poppy seeds using a
polyvalent alcohol, such as e.g. propylene glycol, at 20-50°C,
optionally in a vacuum.

30 Further, it is preferred that the conditioned extract from
Mentha be an extract from *Mentha aquatica*, *Mentha arvensis*,
Mentha piperita, *Mentha pulegium*, *Mentha rotundifolia*, *Mentha*
viridis or mixtures thereof containing *Mentha* in an amount of
approx. 0.5 % by weight relative to the total weight of the
35 conditioned extract, which can additionally contain water,
stabilizers and preservatives (INCI: Water & *Mentha piperita*
leaf extract). The extraction is done at 20-50°C.

The extracts from Passiflora, e.g. *P. incarnata*, and from Myrtus, e.g. *M. communis*, *M. communis* 'Flore Pleno', *M. communis* ssp. *tarentia*, are extracts obtained from the flowers using propylene glycol (PPG) at temperatures of 20-50°C. The specific amounts contained in the conditioned extract are approx. 2-3 % by weight relative to the total weight of the conditioned extract, which can additionally contain water, PPG and preservatives (INCI: Water & Passiflora incarnata flower extract and Water & Myrtus communis flower extract, respectively).

The myrtle extract (e.g. *Myrtus communis*) is an aqueous-alcoholic or purely alcoholic extract from flowers and leaves, the alcohol used being a polyvalent alcohol, such as propylene glycol, and the extraction being done at 20-50°C.

The texture of the inventive cosmetic is such that the O/W emulsion transforms into a gel when being applied to and rubbed slightly into the skin, bringing about a particularly soft feel. There is no stickiness at all. Overall, a kind of Botox effect is achieved, which, however, manifests itself in a reduction and flattening of wrinkles and makes the skin look young.

In addition, it has been found that the skin's elasticity improved by up to 40 % following 4 weeks of treatment. A test lasting for 8 hours and a long-term study carried on for 4 weeks showed that much moisture is retained, so that on the whole a significant long-lasting effect has been found for this composition of the invention.

Altogether, a skin-smoothing effect has been observed for the inventive cosmetic, which could not be expected from the individual ingredients. In particular, the silky texture is achieved without adding the usual pigments or powders, i.e. these can be omitted completely.

The inventive cosmetic further contains cosmetic auxiliaries and carriers as they are commonly used in such preparations, e.g.

water, preservatives, colourants, thickeners, fragrances, alcohols, polyols, esters, electrolytes, gel-forming agents, polar and non-polar oils, polymers, copolymers, emulsifiers, waxes, stabilizers.

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It is particularly preferred that antioxidants and free radical scavengers be added. These substances include vitamins such as vitamin C and derivatives thereof, e.g. ascorbyl acetate, ascorbyl phosphate and ascorbyl palmitate; vitamin A and deriva-
 10 tives thereof; folic acid and derivatives thereof; vitamin E and derivatives thereof such as tocopheryl acetate; flavons or flavonoids; amino acids such as histidine, glycine, tyrosine, tryptophan and derivatives thereof; carotenoids and carotenes such as e.g. α -carotene, β -carotene; uric acid and derivatives
 15 thereof; α -hydroxy acids such as citric acid, lactic acid, malic acid; stilbenes and derivatives thereof; and mixtures of the aforesaid substances.

In particular, the inventive silicone oil system consists of a
 20 combination of silicone oils with a silicone gel. Silicone oils which are advantageously used are e.g. cyclohexasiloxane, cyclopentasiloxane, cyclotetrasiloxane, dimethicone and mixtures thereof.

25 Silicone oils preferably make up between 5 and 15 % by weight relative to the cosmetic's total weight.

Combinations of these silicone oils with silicone gels are e.g. those with Dimethicone & PEG 10 Dimethicone Crosspolymer &
 30 PEG 15 Dimethicone Crosspolymer (73:13.5:13.5) or with Dimethicone & PEG 10 Dimethicone Crosspolymer & PEG 15 Dimethicone Crosspolymer (73:13.5:13.5).

The inventive cosmetic can contain emulsifiers for preparing the
 35 O/W emulsions. Suitable emulsifiers for O/W emulsions are e.g. addition products of 2-30 moles ethylene oxide to linear C_8 - C_{22} fatty alcohols, to C_{12} - C_{22} fatty acids and to C_8 - C_{15} alkyl phenols; C_{12} - C_{22} fatty acid monoesters and diesters of addition

products of 1-30 moles ethylene oxide to glycerine.

As described above, no pigments need to be added. If desired, however, pigments, pigment mixtures or powders having a pigment-like effect can be added as cosmetic auxiliaries, but this is not preferred. These also include those with a pearlescent effect. These pigments or powders can e.g. be silicon dioxide, iron oxides, natural aluminosilicates such as ochre, titanium (di)oxide, mica, kaolin, clays containing manganese such as
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umber and red bole, calcium carbonate, talcum, mica-titanium oxide, mica-titanium oxide-iron oxide, bismuth oxychloride, nylon globules, ceramic globules, expanded and non-expanded synthetic polymer powders, powdery natural organic compounds such as ground solid algae, ground parts of plants and mica-titanium oxide-organic colourant.

Polyols can also be contained in the inventive cosmetic. These are e.g. propylene glycol, dipropylene glycol, ethylene glycol, isoprene glycol, glycerine, butylene glycol, sorbitol and
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mixtures thereof. The polyol makes up between 0.1 and 40 % by weight, preferably between approx. 5 % and approx. 20 % by weight of the gel composition.

Another additive for the inventive cosmetic is an active preparation with a high radical protection factor, containing a product obtained by extracting the bark of Quebracho blanco and subsequent enzymatic hydrolysis, which product contains at least 90 % by weight proanthocyanidine oligomers and max. 10 % by weight gallic acid, in microcapsules, and a silkworm extract
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obtained by extraction, which extract contains the peptide cecropine, amino acids and a vitamin mixture, and a non-ionic, cationic or anionic hydrogel or hydrogel mixture, and one or several phospholipid(s) and water. This is e.g. an active complex according to Example 1 or 2 of WO 99/66881 or e.g. an active complex according to Example 1 of WO 01/26617. Surprisingly, the addition of the aforesaid active preparation to the inventive combination considerably improves the effect of the latter as regards its free radical scavenging properties (e.g.

radical protection factor RPF of the active complex of Example 2 of WO 99/66881 = 2,120; RPF of the inventive extract combination in Example 1 = 840; RPF of the active complex plus the extract combination = 3,230 radicals·10¹⁴/mg).

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Moreover, the inventive cosmetic can advantageously contain suitable water- and/or oil-soluble UVA or UVB filters or both. Advantageous oil-soluble UVB filters include derivatives of 4-aminobenzoic acid such as 4-(dimethylamino)-benzoic acid-(2-ethylhexyl) ester; esters of cinnamic acid such as 4-methoxy cinnamic acid(2-ethylhexyl) ester; benzophenone derivatives such as 2-hydroxy-4-methoxy benzophenone; derivatives of 3-benzylidene camphor such as 3-benzylidene camphor.

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Preferred oil-soluble UV filters are benzophenone-3, butyl methoxybenzoylmethane, octyl methoxycinnamate, octyl salicylate, 4-methylbenzylidene camphor, homosalate and octyl dimethyl PABA.

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Water-soluble UVB filters are e.g. sulphonic acid derivatives of benzophenone or of 3-benzylidene camphor, or salts such as the Na salt or K salt of 2-phenylbenzimidazol-5-sulphonic acid.

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UVA filters include derivatives of dibenzoylmethane such as 1-phenyl-4-(4'-isopropylphenyl)propane-1,3-dione.

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The inventive cosmetic compositions can e.g. be used in the form of suncreams, sun gels, after-sun products, day creams, night creams, masks, body lotions, cleansing milk, body powder, eye cosmetics, hair masks, hair conditioners, hair shampoos, shower gels, shower oils, bath oils and in decorative cosmetic products such as deo sticks, perfume sticks, lipsticks, gels, eyeshadows, compact products such as compact powder or compact wax, rouge, foundation, make-up, etc. The aforesaid products are manufactured in a way known to those skilled in the art.

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Creams, gels, masks, lotions, eye cosmetics, make-ups are particularly preferred since these forms of application are in most cases applied regularly. The effects achieved, i.e. a

reduction or flattening of wrinkles, can e.g. be seen in the photos. Noticeable improvements can already be observed after 7 days of applying the respective product to the facial skin twice a day.

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The invention will now be explained in more detail by means of examples. All quantities are in per cent by weight unless indicated otherwise.

10 In the attached drawing,
Fig. 1: shows a photo of a skin area treated in vivo with the cream according to Example 2, (A) prior to treatment and (B) after 7 days of treatment.

15 Example 1 **Skin cream for normal skin**

Phase A

| | |
|------------------|-------------|
| Water | up to 100 % |
| Glycerine | 3.0 |
| Propylene Glycol | 3.0 |

20 **Phase B**

| | |
|---|------|
| Silicone Gel (Dimethicone & PEG 15 Dimethicone Crosspolymer) | 4.8 |
| Dimethicone Silicone | 11.0 |

Phase C

| | |
|--|------|
| 25 Vitamin Mixture (B ₂ , B ₆ , B ₁₂ , C, E, D) | 1.0 |
| Ethanol | 5.0 |
| RPF Complex* | 0.5 |
| Mentha Extract | 2.5 |
| Passiflora Extract | 0.5 |
| 30 Papaver Extract | 1.0 |
| Myrtus Extract | 0.5 |
| TiO ₂ | 0.5 |
| Vitamin A Palmitate | 0.05 |
| Perfume | 0.5 |
| 35 Preservative | 0.5 |

* Active complex according to Example 1 of WO 99/66881

Phases A and B were prepared separately and, in doing so, both were heated to approx. 80°C. The two phases were combined with one another while stirring and homogenized for 20 minutes. The mixture was cooled down to 60°C, homogenized for approx. 5 minutes, then cooled down to 50°C and homogenized for another 5 minutes. Subsequently, the mixture was cooled down to 35°C and Phase C, which had been prepared separately at temperatures below 35°C, was added and homogenized for some minutes again.

Example 1a

0.8 % of the hexapeptide acetyl-Glu-Glu-Met-Gln-Arg-Arg-NH₂ was added to Phase C.

Example 2 **Body cream I**

Phase A

| | |
|------------------|-------------|
| Water | up to 100 % |
| Glycerine | 10.0 |
| Propylene Glycol | 3.0 |

Phase B

| | |
|--|------|
| Silicone Gel (Dimethicone & PEG 10 Dimethicone Crosspolymer) | 5.8 |
| Dimethicone Silicone | 12.0 |

Phase C

| | |
|---------------------|------|
| Vitamin Mixture | 1.0 |
| Alcohol | 10.0 |
| RPF Complex* | 0.5 |
| Mentha Extract | 2.0 |
| Passiflora Extract | 0.3 |
| Papaver Extract | 2.0 |
| Myrtus Extract | 1.5 |
| Vitamin A Palmitate | 0.5 |
| Perfume | 0.5 |
| Preservative | 0.5 |

* Active complex according to Example 2 of WO 99/66881

Processing was done as in Example 1.

Example 2a

1.3 % of the hexapeptide was added to Phase C.

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Example 3 **Cream for dry skin**

Phase A

| | |
|---------------------|-------------|
| Water | up to 100 % |
| Glycerine | 5.0 |
| 10 Propylene Glycol | 3.0 |

Phase B

| | |
|--|------|
| Silicone Gel (Dimethicone & PEG 10 & PEG 15 Dimethicone Crosspolymer) | 6.9 |
| Dimethicone Silicone | 14.8 |

15 **Phase C**

| | |
|--|-----|
| Vitamin Mixture | 1.0 |
| Alcohol | 8.0 |
| RPF Complex* | 0.8 |
| Mentha Extract | 2.5 |
| 20 Passiflora Extract | 0.5 |
| Papaver Extract | 1.2 |
| Myrtus Extract | 0.5 |
| TiO ₂ /SiO ₂ Pigment | 0.5 |
| Vitamin A Palmitate | 0.1 |
| 25 Perfume | 0.5 |
| Preservative | 0.5 |

* Active complex according to Example 1 of WO 01/26617
Processing was done as in Example 1.

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Example 3a

1.5 % of the hexapeptide and 1.1 % of the RPF complex according
to Example 2 of WO 99/66881 were added to Phase C.

35 Example 4 **Body cream II**

Phase A

| | |
|-------|-------------|
| Water | up to 100 % |
|-------|-------------|

| | | |
|----|--|------|
| | Glycerine | 10.0 |
| | Propylene Glycol | 3.0 |
| | Phase B | |
| 5 | Silicone Gel (Dimethicone & PEG 10 & PEG 15 Dimethicone Crosspolymer) | 5.8 |
| | Dimethicone Silicone | 12.0 |
| | Phase C | |
| | Vitamin Mixture | 1.0 |
| | Alcohol | 10.0 |
| 10 | Hexapeptide* | 1.0 |
| | Mentha Extract | 2.0 |
| | Passiflora Extract | 0.3 |
| | Papaver Extract | 2.0 |
| | Myrtus Extract | 1.5 |
| 15 | Vitamin A Palmitate | 0.5 |
| | Perfume | 0.5 |
| | Preservative | 0.5 |

* Acetyl-Glu-Glu-Met-Gln-Arg-Arg-NH₂

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Processing was done as in Example 1.

Example 4a

No hexapeptide was added to Phase C.

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Example 5 **Comparative test regarding moisture improvement**

The moisture in the skin of 18 female test persons with dry mixed skin was measured using a corneometer. The measurements were taken with a Corneometer CM 825 (Courage & Khazaka, Germany) at 22°C and 56 % relative air humidity. The different creams were applied 2 hours after the skin had been cleansed. The following table shows the results as regards moisturizing in % as average values.

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Table 1

| Time | Cream of Example 1 | | Cream of Example 2a | | Cream of Expl. 1 without extracts | |
|---------|--------------------|----------|---------------------|----------|-----------------------------------|----------|
| | Average | Increase | Average | Increase | Average | Increase |
| before | 42.5 | - | 40 | - | 42.5 | - |
| 0.5 h | 58 | +36 % | 51 | +28 % | 52 | +22 % |
| 2 h | 58 | +36 % | 53 | +33 % | 53 | +24 % |
| 6 h | 56 | +32 % | 54 | +35 % | 52 | +22 % |
| 24 h | 60 | +41 % | - | - | 45 | + 5 % |
| 2 weeks | 62 | +45 % | 59 | +48 % | - | - |
| 4 weeks | 65 | +53 % | 63 | +54 % | - | - |

5 The comparison shows that the cream according to Example 1 of
 the present invention containing the aforescribed complex
 has a moisturizing effect which is noticeably better than that
 of a cream without this complex. The comparative cream without
 the complex still showed an increased moisture value after
 8 hours, but fell to nearly zero after 24 h, while the inven-
 10 tive cream had increased moisture values of +41 %. It is
 particularly significant that these values are maintained and
 even increased over a period of time of 4 weeks.

15 Example 6 Comparative tests regarding the anti-wrinkle effect
 Tests were carried out in order to prove the anti-wrinkle
 effect. The test included 21 male and female test persons aged
 between 42 and 61 years. A microrelief of parts of the facial
 skin (eye area, corners of the mouth, nose area) was taken using
 a silicone mass, said mass was left to harden and the negative
 20 relief obtained was measured electrooptically as regards the
 depth and number of wrinkles. Immediately after the microrelief
 had been taken, a cream was applied to the face of the test per-
 sons for the first time, which cream was then applied repeatedly
 twice a day in an amount of approx. 2 g/cm².

- Group 1: 12 test persons were treated with the cream of Example 1;
- Group 2: 6 test persons were treated with the cream of Example 2a;
- 5 Group 3: 3 test persons were treated with a cream which consisted only of the basic formulation of Example 1 without active agents (placebo).

10 Control measurements were carried out on the 14th and 28th day after the first measurement by taking the microrelief of the same skin areas of the individual test persons. During this time, no test person was subjected to particularly intense solar radiation. The values determined are statistical average values for a selected area of the microrelief.

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Table 2

| | Number of test persons | | |
|--|------------------------|---------|---------|
| | Group 1 | Group 2 | Group 3 |
| Reduction of wrinkle depth after 14 days | | | |
| by 10 - 30 % | 8 | 4 | 1 |
| by 30 - 50 % | 4 | - | - |
| Reduction of wrinkle depth after 28 days | | | |
| by 10 - 30 % | 2 | 1 | 1 |
| by 40 - 50 % | 7 | 3 | - |
| > 50 % | 2 | 2 | - |

20 Group 1 shows a very good reduction of the wrinkle depth after 28 days for 75 % of the test persons. Compared to Group 1, the inventive composition according to Example 2a, tested in Group 2, shows a significant additional improvement, which can be put down to the interaction with the hexapeptide.